Operative Surgery for Enterocutaneous Fistula

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ABSTRACT

The management of the patient with an enterocutaneous fistula is complex and requires coordinated care on many fronts for successful elimination. With optimal non-operative management a fistula may heal spontaneously, the majority within the first 4 weeks after development. Definitive surgical treatment is best achieved with resection of the bowel containing the fistula and anastomosis of healthy normal bowel. The timing of definitive surgery appears to be optimal months after development, if tolerated. Death rates are low after surgery and patients who experience the recurrence of a fistula after initial attempt at closure can ultimately still be cured.

KEYWORDS: Enterocutaneous fistulas, operative management, timing, resection

Objectives: At the completion of this article, readers should be able to identify the critical steps required and outcomes expected for operative management of an enterocutaneous fistula.

The surgeon treating a patient with an enterocutaneous fistula (ECF) is faced with a daunting challenge, yet one that can be successfully overcome when knowledge, judgment, and technical skills are judiciously combined. Overall care of the ECF patient synchronously requires a mastery of gastrointestinal (GI) radiology, infectious disease, nutrition and electrolyte management, as well as an ability to provide emotional support to a patient and family over what will be a prolonged treatment course. Surgical management also requires patience, a skill not inherent to the surgical personality. The documented decrease in mortality and improved healing rates over recent decades of patients suffering from ECF demonstrates the importance of such multimodality therapy.

As pointed out by Drs. Lundy and Fischer in the opening article, the evolution of care for patients with ECFs over the past 50 years has demonstrated some significant developments that have led to the recognition of certain principals to minimize morbidity and mortal-

ity. Dr. Claude Welch and colleagues in 1960 reported on a series of patients with fistulas, while making the connection between proper nutrition, identification of septic foci, and minimizing mortality. In describing those with high-output small bowel fistula, the authors noted "Seventy-four per cent of these patients suffered significant malnutrition...and 59 per cent of these malnourished patients died. Only four of these patients, all with jejunal fistulas, had any tube feedings. Sepsis was a major complication of these fistulas. There were 55 separate infections in 46 patients. Fourteen patients developed generalized peritonitis and 10 (72%) died. The large number of intraperitoneal abscesses that occurred, or which first were discovered after the formation of the fistula, emphasized the need of careful search for this complication in patients with fistulas."¹ The development of parenteral nutrition was one of the next major advances in the care for these patients. Fischer and colleagues in the 1970s described the impact of hyperalimentation and peri-operative care in patients with GI

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fistulas.² The combined improvements in care resulted in a mortality decrease among patients with GI cutaneous fistulas from ~48% to 15%. By the 1980s, a well-focused paradigm was accepted that incorporated sepsis control, wound care, nutritional support, and stress on operative technique—concepts that remain critical to this day. Such an overall treatment plan delivered improved rates of fistula elimination.³

Nevertheless, the surgeon still plays a critical leadership role in the management of these patients. In addition to the technical considerations, specific and successful operative management of the ECF involves decision making in a number of areas. Among these, one must first determine how long to wait for closure of a fistula before undertaking an operation and understand the differences in behavior of proximal versus distal fistulas. In the operating room, principles of proper dissection and resection that have been studied must be applied. Finally, surgical providers must be cognizant of possible complications and be ready to manage issues such as the recurrent fistula following resection.

TIMING OF OPERATION

Spontaneous Closure of Fistulas

Spontaneous closure rates of ECFs following optimal nonoperative therapy range widely depending on the cause of the fistula, and other variables including nutrition, location, and comorbidities. When postoperative small bowel fistulas were specifically examined in 2008 by Martinez and colleagues, only 25% resulted in spontaneous closure (23 of 90 patients).⁴ Though multiple factors ultimately play a role in successful nonoperative closure, the authors found source control and elimination of sepsis as independent variables that were essential to promote spontaneous closure. In this study, spontaneous closure rates for patients without sepsis were almost double the rate of those with sepsis (49% vs 26%, respectively). These rates significantly diminished (10%), if closure was not achieved 1 month after sepsis control.

Univariate and multivariate analysis of factors related to spontaneous closure was performed by the Martinez group, identifying jejunal site, high output, multiple fistulas, and development of sepsis as factors that precluded spontaneous closure on univariate analysis. After multivariate analysis, multiple (vs a single fistula) postoperative enterocutaneous fistula (PECF) almost achieved statistical significance against spontaneous closure ($p = 0.06$), whereas statistical significance was achieved for high-output and jejunal site. Overall, odds ratios were calculated and chances for spontaneous closure were 3.5 and 2.5 times lower for jejunal and high-output PECF, compared with other sites of origin and low-output PECF, respectively. The only factor that

avored spontaneous closure was that the fistula was developed at their hospital. Often, patients with PECF that originated at other institutions who were referred to their institution did not experience spontaneous closure, though speculation only may be a reason why to include the importance of continuity of care or perhaps intrinsic biases (i.e., more severe cases) related to those patients making up the transfer cohort. Importantly, this group from Mexico found the mean time of spontaneous closure of fistulas from time to discovery or initial treatment at their institution to hover around 30 days: jejunal origin 30 days (20 to 50), ileal 28 days (14 to 60), colonic 30 days (10 to 180). The wide range of timing brings to light the patience that both the patient and surgeon must have, as well as the not-infrequent spontaneous closure—even despite longer intervals (especially with colonic sources).

Interestingly, over 30 years ago the surgical team from the University of California Medical Center, San Francisco evaluated their experience with 186 patients with external GI fistulas treated from 1968 to 1977 and found similar results.⁵ Like the Martinez group, in their experience spontaneous closure could not be expected to start until sepsis was controlled. After infection was eradicated, over 90% of patients whose fistulas closed spontaneously did so within the next month. Less than 10% of fistulas closed in the 2 months thereafter (i.e., in the second and third months after control of sepsis). Therefore, the importance of evaluating for hidden sources of infection, especially in those with recalcitrant disease, cannot be overemphasized.

More recently, the specialized surgery unit at St. Marks Hospital in the United Kingdom published an 11-year retrospective review of their experience with ECF through 2004.⁶ Utilizing optimal nonoperative therapy, spontaneous healing was observed in 19.9% of patients. The spontaneous closure rate was lower than that in many other reported series, perhaps reflecting the complex group of patients, many of whom were referred from other centers after failure of fistula healing. Of their patients, fistulas resulted from surgery in 235 (84.8%) of the 277 patients. Of these, 111 (47.2%) had inflammatory bowel disease (76 Crohn disease and 35 ulcerative colitis) and 14 (6.0%) had had previous radiotherapy. The St. Mark's Intestinal Failure Unit has had a long-standing interest in inflammatory bowel disease, reflected in the relatively high prevalence of Crohn disease in this cohort. In attempting to determine factors associated with successful or unsuccessful closure, the authors found the presence of active inflammation, owing to coexisting inflammatory bowel disease, granulation tissue, or sepsis have predisposed to fistula formation, failure to heal, or refistulization.

Though it has been over 40 years since Welch's landmark article,¹ the authors found early recognition and control of sepsis, management of fluid and electrolyte

imbalances, meticulous wound care, nutritional support, and the delay of definitive surgery for at least 6 months resulted in low mortality rates in their series of patients with ECF—concepts that have remained to this day. A higher mortality rate was observed in patients treated nonoperatively, reflecting their critical medical state before stabilization and consideration for subsequent surgery. The authors believed that the multidisciplinary care provided for these patients was of great importance, with team members investing significant amounts of time and resources in their management.

Timing of Definitive Operative Intervention

Certainly the patient with enteric content exiting a wound on their abdomen is motivated to undergo operation. In 2004, the Cleveland Clinic reported their retrospective evaluation of the records of patients who had ECF surgery between 1994 and 2001.⁷ In their thoughtful study, the colorectal surgery group reported a large series of ECFs at a tertiary-referral unit and used multivariate analysis to examine patient and surgical-related factors that affect fistula recurrence rates after surgery. In general, the authors attempted uniform management as much as possible. Principles that were followed for the management of fistulas in these patients included preoperative antibiotic, thromboprophylaxis, and drainage of abscesses by computerized tomography with later surgery once the acute process was resolved and the patients were in better physiological condition. This group strived to answer questions that would enable improvement in the care of the ECF patient. The median time to definitive repair from fistula onset was 6 months (range, 1 day to 28 months). Those patients operated on between 2 and 12 weeks after their last surgery had an ECF recurrence rate of 28% (10 of 36). This was higher than those patients whose operation was delayed longer than 12 weeks (recurrence rate 15% 17 of 114, $p = 0.088$, Fisher exact test). Logistic regression analysis was used to generate a probability of fistula recurrence after definitive surgery relative to time since fistula onset and suggested that delaying surgery resulted in a higher chance of successful outcome.

The 6-month time course is commonly utilized by groups with significant experience treating fistulas, owing to the trend in encountering a less hostile abdomen than in the early phases. Similar to the Cleveland Clinic experience, the St. Marks' group delayed definitive surgery for a median of 8 (range 1 to 180) months after the occurrence of fistulation or previous major operation.⁵ Though there is no definitive data suggesting the exact timing for reexploration, it appears that unless certain conditions are present requiring more emergent surgical intervention, due diligence with longer intervals and maximal optimization is a critical component to success.

Surgery to control sepsis is obviously administered promptly and on an individualized basis, mainly in the setting of uncontrolled fecal spillage or anastomotic leaks. Source control and elimination of sepsis are essential steps in the initial management of the ECF, and the patient's clinical condition and risk profile needs to be considered when determining the need for more urgent exploration versus nonoperative care. Even though source control may be achieved by nonsurgical means, some patients may require prompt or immediate operative intervention upon fistula development. Dr. Orangio further explores the various clinical presentations of ECFs and their impact on timing and management elsewhere in this issue.

Operative Technique

The technical care required to eradicate the ECF is significant. Principles include careful and sufficient adhesiolysis, meticulous hemostasis, and proper tissue handling to prevent unnecessary and inadvertent enterotomy, as well as enable resection of the fistula. Primary anastomosis with or without proximal diversion can then be created depending on patient factors and surgeon judgment. These operations demand a surgical team's full attention and cannot be rushed. In addition to ensuring a thorough and detailed preoperative workup, once the decision has been made to proceed to the operating room, an appropriate operative plan that entails dedicating sufficient operative time for the procedure is just as critical.

The operation truly begins with positioning. Access to the anus is helpful as it can permit intraoperative endoscopy. I prepare for the difficult operation with the patient in stirrups. Depending on the patient's prior disease or surgical history, a low threshold for ureteral stent placement should be maintained. The abdominal wall can be prepared to minimize direct flow of enteric content into the surgical field from the fistula. If possible, an adhesive transparent skin drape can be placed over the prepped abdominal skin and then incised as needed during the course of the operation. Some surgeons will "plug" or cover the fistula with gauze prior to the placement of the adhesive adherent skin barrier.

Entering the abdomen of the fistula patient can be extraordinarily difficult. The skin incision should start above the prior incision, with the goal to perhaps enter a "free space" where bowel is not adherent to the abdominal wall. The surgical saying, "when surgery gets difficult, go to someplace easy... and then what is hard may become easier" has extra importance when fistula surgery is performed. Graham Hill in his important work, "Operative Strategy in the Treatment of Enterocutaneous Fistula" from 1983 describes the painstaking technique of dissecting free the small bowel to prepare for resection.⁸ "Dissection is carried under the abdominal

scar, which is progressively opened, and far out into both flanks, separating the peritoneum widely up to the area where the bowel is densely adherent around the site at which the fistula passes to its opening on the surface. During the course of this dissection, an identifiable loop of small bowel is sought, although frequently in difficult cases it may only be found far on in the course of the dissection and located well laterally in one of the colic gutters. . . . Once a coil of intestine has been identified, the painstaking task of dissecting the entire length of small intestine, both proximal and distal to the fistula can proceed." Sharp dissection eliminates the risk of unrecognized thermal injury to intestine. Although some surgeons may not be as experienced or comfortable working with a surgical blade alone, this is often one of the few scenarios where it is critically important to mobilize "frozen" loops of bowel from the undersurface of the abdomen. Ultimately one arrives at the intestine that is more densely adherent to the abdominal wall and that contains the fistula itself. The skin adjacent to the fistula is incised through all layers of the abdominal wall so the entire fistula complex can be excised. Division of healthy bowel both proximal and distal to the fistula is performed and tension-free anastomosis created.

Though the principle of resection of the fistula with primary anastomosis has been recommended in even the earliest surgical works on fistula,^{1,2} the Cleveland Clinic evaluation of their experience with various techniques for definitive treatment of ECF is particularly illuminating. The Cleveland unit found surgical repair technique was a significant predictor of ECF recurrence. Patients with a wedge repair or oversewing of an ECF had a recurrence rate of 32.7%, compared with 18.4% if the ECF was resected or the anastomosis revised ($p=0.004$, Fisher exact test). No patient who had both a wedge repair and resection had ECF recurrence. If only a wedge repair/oversewing or resection was performed ($n=198$), resection only resulted in a better outcome with a recurrence rate of 17% (26 of 154) compared with 36% (16 of 44) for those oversewn only ($p=0.011$ Fisher exact test). Resection technique was also important in the Crohn disease subgroup. Analysis showed oversewing resulted in a recurrence rate of 75% (9 of 12) compared with a recurrence rate of 15% (12/83) for those resected ($p=0.0001$, Fisher exact test). Crohn disease by itself did not influence recurrence (recurrence rate = 22%, $p=0.73$, Fisher exact test). A multivariate logistic regression model was then constructed, which also identified oversewing or wedge repair as a primary predictor of recurrence.⁷ The Cleveland Clinic authors note that in some cases, a fistula may have been oversewn when it was not thought possible to perform a resection. This may have been because of an inability to adequately mobilize the bowel or concerns about the possibility of short bowel syndrome. If this is the situation, consid-

eration should be given to protecting the repair with a proximal stoma or performing a bypass of that area. However, based on their experience, every attempt should be made to avoid simple oversewing. The importance of complete resection and anastomosis was specifically remarked upon by the St. Marks group, "All diseased bowel was resected and reanastomosis only performed between healthy ends, irrespective of the amount of bowel lost."⁵ Although initially it may be appealing to avoid bowel resection, especially in those with concerns for current or future short bowel development, improper handling of the fistula with recurrence may ultimately prove to be more devastating.

Outcomes

The most important outcomes in the care of the patient with an ECF include eradication of the fistula and issues regarding patient safety. Single institution reviews from referral centers currently provide the best available data to assess the state of the art.

The most recently published retrospective review is that of the previously referred to Martinez and associates' evaluation from Mexico in 2008.⁴ In this work, the authors specifically focused on PECF. Overall, PECF closure was obtained in 151 patients (86%); a total of 65 (37%) had spontaneous closure, and the remaining 86 (49%) healed through operative means. Surgical closure was achieved in 59 of the 64 patients (92%) undergoing fistula resection and primary anastomosis, 13 of 16 (81%) after resection and a diverting ostomy, 7 of 10 (70%) after primary PECF closure, and 7 of 12 (58%) after abscess drainage. Twenty-three patients (13%) died; 16 of them (70%) had been submitted to operative treatment, and 14 (61%) had jejunal PECF. Several variables were significantly associated with mortality through univariate analysis, which included serum albumin <3 g/dL, fluid and electrolyte imbalance at the moment of diagnosis or referral, development of sepsis, jejunal site, high output, complex fistulous tract, and multiple fistulas. After multivariate analysis, however, only jejunal site, multiple PECF, and development of sepsis prevailed as independent significant factors with death.

The report from the Cleveland Clinic of 2004 similarly reports an ultimately high rate of fistula elimination and low mortality rate.⁷ Two-hundred three patients had a definitive surgical procedure for ECF. Forty-two (21%) had recurrence within 3 months, including three patients after subsequent complications, and one after stoma closure. There were 170 patients with PECF who had definitive surgery performed; 31 (18%) had fistula recurrence. This was not significantly different from those with spontaneous ECF (11 of 35 patients, 31%, $p=0.11$, Fisher exact test). One-hundred nineteen (58%) of the 205 patients had one procedure only. Of these, 36 still had a stoma and three patients had an

ongoing ECF at the time of publication (etiologic factors: necrotizing pancreatitis, radiation for intraabdominal desmoid drained only and subsequently died, and Crohn disease). The other 86 patients had subsequent surgical procedures. Thirty-one of the 89 patients (35%) with defunctioning or end stomas had these closed or rejoined. One of these 31 patients had a recurrence of ECF (carcinoid, initially oversewn, and defunctioned) without subsequent treatment. Six patients died within 3 months of definitive surgical management. Death was due to cardiac complications in one, respiratory complications in two, multiorgan failure in two, and a variceal bleed in one patient. One of these patients had a recurrence of ECF prior to death.

The work of the St. Marks group further illustrates the positive outcome that can be derived from a coordinated stepwise approach.⁶ The study also specifically illustrates that elimination of fistulas that occur after initial treatment failure can be similarly successfully managed. The final fistula healing rate produced by this group after definitive surgery was 82.0% (137 of 167). After definitive surgery, fistula healing occurred in 107 (64.1%), refistulation occurred in 55 patients and five patients died. Fourteen patients with refistulation were treated conservatively, resulting in spontaneous closure in a further eight patients; one patient who died from pneumonia 4 months later still had a fistula and the remaining five patients had ongoing fistulas. Of the remaining 41 patients with refistulation, 21 had definitive repeat fistula resection and 20 had surgery to control sepsis. Of those who had repeat resection, fistulas healed in 14, two died after surgery and five had ongoing recurrent fistulation (including a patient who underwent two further attempts at operative closure). Fistula-related complications accounted for an overall mortality rate of 10.8% (30 of 277); 23 of the 30 were attributed to sepsis. Six of the 30 deaths occurred within 30 days of major surgery, five after definitive fistula surgery and one after laparotomy for sepsis.

Finally, in 2010 the first prospective study of ECF treatment was reported. The results were from a regional unit in the United Kingdom.⁹ The treating physicians utilized the management paradigm described here including waiting at least 6 months from the time of fistula development. Definitive surgery was, in fact, delayed in their patients for a median of 9 (range, 6 to 48) months after previous major surgery or the occurrence of a fistula. In total, 35 of 42 patients had successful fistula healing. Four patients healed spontaneously and 31 patients healed after surgery (including the 10 patients who had reversals of defunctioning stomas after definitive surgery). Four patients (11%) developed a recurrent fistula at the site of anastomosis after surgery. Only one of these patients required further surgery, whereas the other

three healed spontaneously. No patients were left dependent on parenteral nutrition after definitive surgery. The overall mortality of this series was 7% (4 of 55 patients). Three of the four deaths occurred before definitive surgery. This study illustrates the increasing success of modern therapy for ECF, while still sticking to the basic principles that have withstood the test of time.

CONCLUSION

In conclusion, the surgical management of the patient with an ECF is technically demanding and success depends on both proper intraoperative judgment and thorough preoperative optimization. Although nonoperative management may allow fistulas to heal spontaneously, the majority of those who fail within the first 4 weeks after development will require operative intervention. Ideally, the timing of definitive surgery appears to be optimal several months after fistula development. Despite this, surgeons should be prepared for a difficult and, at times, hostile abdomen. Yet proper reliance on ECF management principles including resection of the bowel containing the fistula and anastomosis of healthy normal bowel can allow for great outcomes with minimal morbidity and mortality.

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